

**Epidemiological and geographical features of cutaneous leishmaniasis in
Southwestern Khuzestan**

Running title: Epidemiological features of cutaneous leishmaniasis in Khuzestan

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Abstract

Background: Cutaneous leishmaniasis (CL) is a protozoan infection caused by a flagellated parasite complex known as *Leishmania* spp. Iran is an endemic area for CL. The present study aimed to investigate the epidemiological factors and geographical distribution of CL in Southwestern Khuzestan using the GIS method.

Methods: In this cross-sectional study, epidemiologic and demographic data from 787 individuals affected by CL in Behbahan County, spanning the years 2002 to 2021, were collected. Patient locations were plotted on a point shapefile of villages, towns, and cities in Behbahan County, and geographic data were analyzed using ArcGIS version 10.

Results: Out of the 787 studied cases, 512 (65%) were male. The disease was most prevalent among individuals aged 21–30. Lesions appeared in various regions of the body, with 41% of cases involving the hands. The highest annual incidence rate was recorded in 2009, at approximately 40 cases per 100,000 population, whereas the lowest incidence rate occurred in 2002, at 5.8 per 100,000 population. Noticeable variations in disease prevalence were identified among non-Iranian individuals, rural populations (including pastoral and peri-urban areas), males, and younger individuals. Geographic Information System (GIS) analysis indicated that the most affected areas were located in the central region (Behbahan or Markazi area) and the southern region (Zeydoon) of the mapped topography.

Conclusion: The findings highlight the necessity of implementing effective prevention and control measures to alleviate the burden of CL in Behbahan County. These measures should include targeted health education campaigns and vector control strategies, with a particular focus on regions identified as high-prevalence areas through GIS topographic analysis.

Keywords: Cutaneous Leishmaniasis (CL), Geographical Features, Geographic Information System (GIS), Epidemiology, Iran

Introduction

Leishmaniasis, a zoonotic disease transmitted by sandflies (*Phlebotomus* spp.) and caused by a group of protozoan parasites known as *Leishmania* spp., manifests in various forms, including cutaneous (CL), mucocutaneous (MCL), and visceral (VL) (1, 2). With approximately 1.5 million new cases per year, this widespread disease poses a risk to more than 100 countries (3). Cutaneous leishmaniasis is particularly prevalent in South America, the Middle East, and North Africa, (2, 4) *L. tropica* and *L. major* being the primary etiological agents in the old world, although other species such as *L. aethiopica*, *L. infantum*, and *L. donovani* have been reported globally to cause CL lesions (5). Leishmaniasis epidemiology is influenced by interactions among the parasite, vector, host, and environment. In Iran, where an estimated 20,000 cases occur annually, the main species responsible for CL are *L. major* and *L. tropica* (6, 7). Zoonotic cutaneous leishmaniasis (ZCL) caused by *L. major* is primarily transmitted to humans in Iran, (8) through *Phlebotomus papatasi* sandflies, while anthroponotic cutaneous leishmaniasis (ACL) (9, 10) caused by *L. tropica* is transmitted between humans through *Ph. sergenti* sandflies, which have also been sporadically identified in dogs (11). The geographic distribution of CL in Iran is wide (12), with *L. major* predominating in the southwest, west, central, and northeast regions, while *L. tropica* is commonly found in the southeast and east, as well as in popular cities such as Shiraz, Mashhad, and Tehran (13). Geographic information systems (GIS) have facilitated the study of the spatial epidemiology of vector-borne diseases. Some GIS-based studies have mapped the leishmaniasis distribution in Iran (14-17). Located in southwestern Iran, the province of Khuzestan is considered one of the country's most significant zoonotic cutaneous leishmaniasis (ZCL) notable points, with Behbahan County being one of its important foci for this disease. (14). The present study aimed to investigate the epidemiological factors and geographical distribution of CL in Southwestern Khuzestan using the GIS method from 2002 to 2021.

Methods

Study area

Behbahan (Figure 1) is one of the twenty-seven counties of Khuzestan province in southwestern Iran (18). The capital of the county is Behbahan City. The county is subdivided into three districts: Central, Tashan, and Zeydun. Also, it consists of four cities: Behbahan, Mansuriyeh, Tashan, and Sardasht (19). Behbahan has a land area of around 3,195 km² and is in the southeast of Khuzestan province at approximately 30° 35' 45"N and 50° 14' 30"E. The population of this county is estimated at 300,000 people (20). Behbahan experiences a hot semi-arid climate, with extremely hot and dry summers and mild winters that can occasionally have heavy rainfall. The average temperature ranges from 42°C during the summer to 35°C, 25°C, and 13°C during autumn, spring, and winter, respectively.



Figure 1. Location of Behbahan county in southwest Iran

Patient and geographical data collection

The data of all CL patients (epidemiologic and demographic data), previously confirmed through microscopic slides and molecular methods in both public and private sectors between 2002 and 2021, were obtained from the Behbahan Health Center. This cross-sectional, descriptive study analyzed demographic and clinical information, including patients' age, gender, occupation, place of residence, month of illness onset, workplace, illness duration, affected counties, nationality, type of wound tissue, lesion morphology, number and size of ulcers, and administered treatments. Statistical analyses were conducted using SPSS software version 21. For spatial analysis, patient locations were mapped using a point shapefile of villages, towns, and cities in Behbahan County. The mapping process was carried out using ArcGIS software version 10.5 (<http://www.esri.com/arcgis>), with the shapefile polygon layer of Behbahan County purchased online from <https://rsgisc.com/>.

Results

Between 2002 and 2021, a total of 708 cases of CL were documented in Behbahan County, with 65% (n=512) of patients being male and 35% (n=275) female. Urban residents constituted 55% (n=433) of the cases, while 45% (n=354) were from rural areas. The highest prevalence was observed among young adults aged 21–30, accounting for 29% (n=226) of cases, whereas the lowest prevalence of 1% (n=9) was found among elderly patients aged over 70. Among patients, 25-year-olds represented the peak prevalence rate of 26.6%. The mean age of male and female patients was 26.1 and 27.3 years, respectively, with 68% of all cases occurring in individuals under the age of 30 (Table 1). Lesions were distributed across various body regions, with 41% of patients experiencing lesions on their hands, 35% on their feet, 18% on their face, 4% on their trunk, and 2% on their neck and head. Approximately 54% of patients presented with a single lesion, and the highest count of lesions observed in one patient was 25. In total, 927 lesions were reported among all cases (Table 2). Regarding occupation, students represented the largest affected group,

accounting for 21% (n=162) of the cases (Table 3). A majority of wounds (61.8%, n=606) were larger than 1 cm in diameter. The study further categorized skin lesions as non-secretory, erythematous, or dry in 65% of cases, while 33% were secretory, and 2% exhibited other wound characteristics (Table 4). The year 2009 recorded the highest number of CL cases (n=75), with the lowest number reported in 2002 (n=10). Seasonally, January (winter) had the highest number of cases (n=125), whereas July (summer) accounted for the lowest (n=23) (Table 5). Annual incidence rates varied from 40 per 100,000 in 2009 to 5.8 per 100,000 in 2002 (Table 6). Regarding treatment approaches, 82% (n=645) of patients received intralesional Glucantime, 13% (n=102) were treated systemically with Glucantime, 4% (n=31) underwent a combination of cryotherapy and Glucantime, and 1% (n=8) received cryotherapy alone. Geographic Information System (GIS) analysis revealed that central areas (Behbahan or Markazi part) and southern regions (Zeydoon) of Behbahan County were the most affected by CL, as indicated by Figure 2.

Table 1. The prevalence of CL among age groups in Behbahan County during 2002-2021

		Age groups							
	1-10y-o*	11-20	21-30	31-40	41-50	51-60	61-70	>70	Total
Frequency	140	165	226	98	70	56	23	9	787
Percent	18	21	29	12	9	7	3	1	100

(*y-o=Years-Old)

Table 2. The prevalence of CL in the place of lesions in Behbahan County during 2002-2021

		Place of lesions					Total
	Hands	Feet	Trunk	Neck and head	Face		
Frequency	375	327	41	22	162	927	
Percent	41	35	4	2	18	100	

Table 3. The prevalence of CL based on occupation in Behbahan County during 2002-2021

		Occupation														Total
	Shepherd	Collegian	Soldier	Military	Staff	Driver	Freelance job	Farmer	Unemploy	Worker	Child	Housewife	Student	Other		
Frequency	8	10	17	24	31	32	49	52	33	79	86	128	162	76	787	
Percent	0.2	1	2.1	3.1	8.3	3.9	6	7	4	10.4	1	16	21	10	100	

Table 4. The prevalence of CL based on the size of lesions in Behbahan County during 2002-2021

		Size of lesions								Total
	≤ 0.5cm	1cm	2cm	3cm	4cm	5cm	6cm	≥ 7cm		
Frequency	355	172	185	98	75	18	19	5	927	
Percent	38.2	18.5	20	10.5	8.1	1.9	2	0.5	100	

Table 5. The prevalence of CL based on the years and months in Behbahan County during 2002-2021

Based on month																				
	April	May	June	July	August	September	October	November	December	January	February	March								
Frequency	51	54	57	23	36	47	52	62	102	125	109	69								
Percent	6.5	6.9	7.2	2.9	4.6	6	6.6	7.9	13	15.9	13.6	8.8								
Based on years																				
	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Frequency	10	50	27	37	39	39	64	75	55	64	23	21	42	37	28	29	31	26	29	61
Percent	1.3	6.3	3.4	4.7	4.8	4.8	8.1	9.5	7	8.1	2.9	2.7	5.3	4.7	3.5	3.7	3.8	3.3	3.7	7.7

Table 6. The annual incidence rate of cutaneous leishmaniasis (CL) per 100,000 population in Behbahan County from 2002 to 2021

The annual incidence rate																					
Year	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	Average
Population	172561	174311	176735	180531	182345	184521	186641	187650	189583	19045	196511	203412	211582	212550	213697	214285	214551	215289	215432	215536	197038
Frequency	10	50	27	37	39	39	64	75	55	64	23	21	42	37	28	29	31	26	29	61	39.3
Incidence	5.8	28.7	15.3	20.5	21.4	21.1	34.3	40	29	33.2	11.7	10.3	19.9	17.4	13.1	13.5	14.4	12.1	13.5	28.3	20

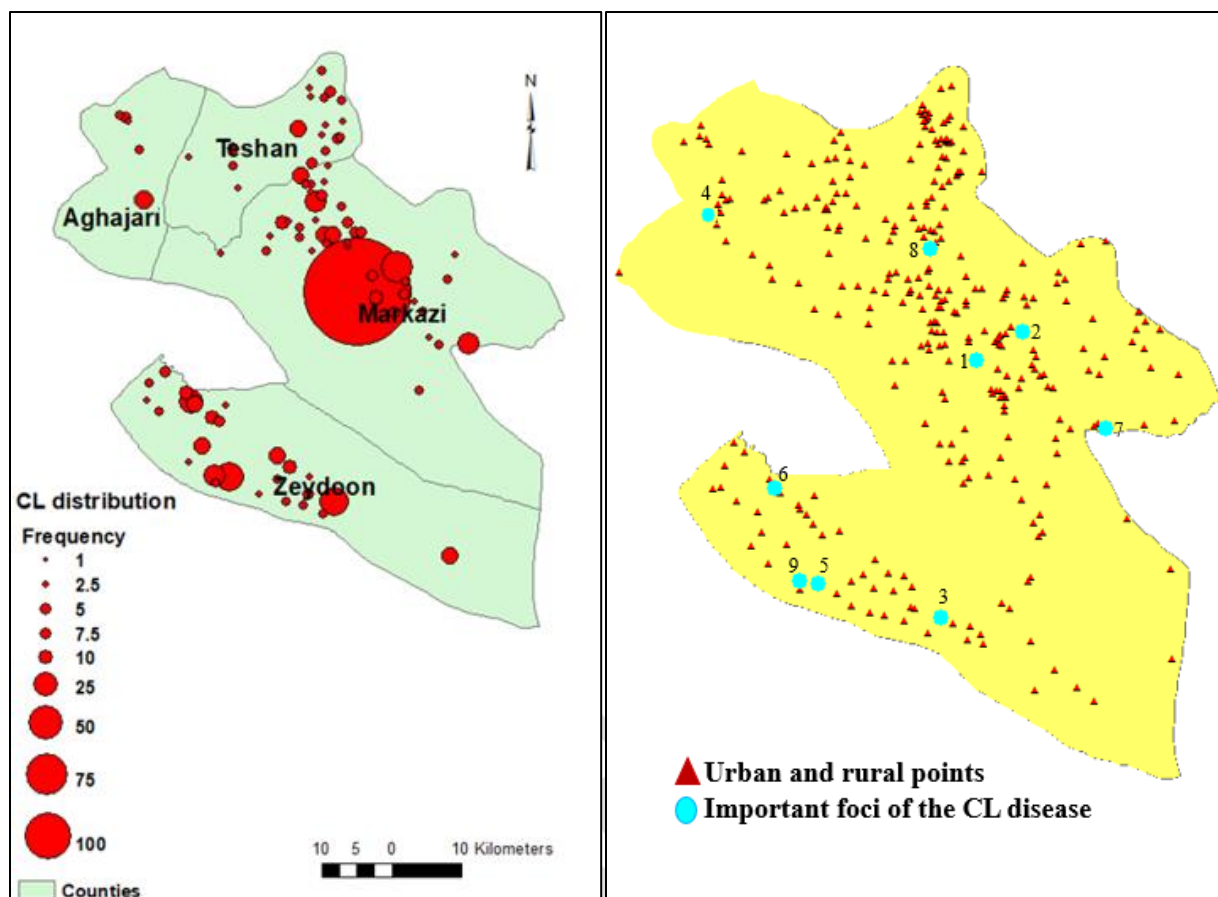


Figure 2. Left (CL distribution map) and Right (Nine important foci of disease). Based on the GIS maps, the most infected counties were the central (Behbahan or Markazi part) and southern (Zeydoon) areas. Behbahan City (point 1 on the right map, n=312 cases) was recognized as the main focus of CL. Other important foci (more than 10 cases reported) shown on the map (Point 2: Mansuriyeh (n=25), 3: Sardasht (n=22), 4: Aghajari (n=21), 5: Darunak (n=21), 6: Longir vosta (n=16), 7: KheirAbad, 8: Dudangeh bozorg, and 9: Julahi (n=11)).

Discussion

Leishmaniasis is classified by the World Health Organization (WHO) as one of the neglected tropical diseases (NTDs)(21). CL is an important health problem with great epidemiological importance in southwestern Iran, which requires effective prevention and control actions (22). This study is the first to survey the distribution pattern of cutaneous leishmaniasis in Behbahan County. The findings revealed that although the disease affected individuals of all ages, a majority of patients were young adults between the ages of 21 and 30. This can be explained by the migration of young people as a workforce to more populated villages and cities and the higher chance of exposure to biting by sandflies regarding the type of job and their socioeconomic level.

In some studies, the prevalence of CL was higher in children under 10 years old (20-22), and in another study, it was dominant in the age group of 30-39 years (23). that didn't agree with the results of the present study. Like most studies in Iran (23-25), in the present study, the disease was more prevalent in men and urban areas (around the cities). Due to men's jobs and activities in open spaces, style of clothing, short-sleeved clothes, and migration to different cities due to their jobs, especially in endemic areas, the prevalence of the disease is higher in men. Unlike the present

study, some studies showed that CL prevalence was higher in women and rural areas. Jafarnejad et al., in their study in Lamerd county, stated that the reason for the higher prevalence of the disease in women is because the men of the family are employed in the Persian Gulf around countries and also the lack of agriculture so that men stay outside in the open space(26-28).

Similar to some previous studies, the results of this study revealed that the majority of bites occurred on the hands. (29-31). In some studies, most bites were reported in both hands and feet (26), some in the face, and some in both the hands and face (27). The hand is one of the uncovered parts of the body and is in direct contact with the environment more than other parts. On the other hand, the oral appendages of the sandflies are shorter than some mosquitoes, like those of the *Anopheles* mosquito, so it is difficult to bite the sites covered by clothing.

The findings of our study indicate that CL exhibited the highest prevalence during the winter months. This pattern may be linked to Behbahan's tropical climate, where the maturation and development of parasites in mosquito vectors occur more rapidly compared to regions with temperate climates. Moreover, zoonotic cutaneous leishmaniasis (ZCL), caused by *Leishmania major*, represents the predominant form of CL in Khuzestan province, including Behbahan County. The average interval between the mosquito bite and the emergence of ZCL as a papule is approximately two weeks (32).

In the study by Namrodi et al. in 2016 in Isfahan province, most cases of the disease were reported in the fall season (33), and in another study in the same province conducted by Barouti-Ardestani, et al. in 2020, the most cases of the disease were reported in the summer season (25). The main reason for this issue is the difference in climatic conditions, environment, ecology, and behavior of vectors in different provinces of the country. In simpler terms, variations in geographical climates result in different transmission patterns and varying impacts of meteorological variables on cutaneous leishmaniasis. It is important to note that while climate change can influence the transmission of leishmaniasis, it is not the sole determining factor. Socioeconomic factors, urbanization, and healthcare infrastructure also play crucial roles in the prevalence and control of the disease (34, 35).

The results of the present study showed that the incidence rate varied between 10 and 75 people per 100,000 population from 2002 to 2021 and has been decreasing over the last 10 years. Reasons for the reduction in the disease's incidence include improved health conditions, environmental enhancements, climate change, and drought, as well as the design and implementation of an annual action plan to combat rodents in key disease areas. Additionally, public and personal health education, along with personal protection measures, have contributed to the decline in Behbahan County. A decrease in the incidence of disease in most regions of Iran has been reported in various studies. Some possible reasons include improved healthcare infrastructure, vector control measures, public awareness and education, urbanization and changes in human behavior, and climate change effects (25, 31, 36).

Geographic Information System (GIS) analysis indicated that the central region (Behbahan) and the southern region (Zeydoon) of the topographic map experienced the highest prevalence of CL. Factors contributing to the elevated prevalence in these areas may include the presence of extensive agricultural lands cultivating crops such as corn, wheat, and barley, which promote the proliferation of rodent populations. Additionally, the combination of humidity and temperature in these regions provides optimal conditions for the breeding and development of ground mosquitoes within rodent nests. Azimi et al. conducted a study on Khuzestan Province, utilizing GIS topographic mapping to identify regions with higher rates of cutaneous leishmaniasis (CL) infection. Their findings revealed that the western and southern parts of the province exhibited

elevated infection rates, which were likely influenced by high temperature and humidity levels (37). Similarly, research by Davoodi et al. on the geographical distribution of CL in Fars Province revealed that anthroponotic cutaneous leishmaniasis (ACL) was exclusively detected in Shiraz city, while zoonotic cutaneous leishmaniasis (ZCL) was prevalent in both Shiraz and most other counties within the province. Notably, the highest concentration of CL cases was reported in district 8 of Shiraz municipality, underscoring the need for targeted interventions in this area (38). Additionally, Khademvatan et al. examined the spatial distribution of leishmaniasis in southwestern Iran, reporting a significant prevalence in the central and western regions of Khuzestan Province. Their study also found that urban areas experienced higher infection rates compared to rural regions (39).

Conclusion

Although the incidence rate of cutaneous leishmaniasis in Behbahan City has been decreasing from 2002 to 2021 and important control and preventive measures have been taken, due to the increase of the disease in some years, this disease remains active as a health and public problem. The results suggest that effective prevention and control measures, including health education campaigns and vector control strategies (especially in areas with high prevalence according to GIS topography), are necessary to reduce the burden of CL in Behbahan County.

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Ethical Statement

This article was supported and approved by the ethics committee of the Behbahan Faculty of Medical Sciences (Code: IR.BHN.REC.1401.012). Patient data was de-identified to protect the privacy and confidentiality of the participants. Additionally, the study was conducted with the utmost respect for the cultural norms and traditions of the participants. Any potential conflicts of interest were disclosed and managed appropriately. The results of the study will be disseminated in a manner that respects the dignity and privacy of the participants and without identifying any individual participants.

Conflict of Interest

None.

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Author Contributions

The study was conceived and designed by Ali Jamshidi and Kazem Alizadeh-Barzian. Data collection was carried out by Abolhasan Difrakhsh, Mehdi Jamshidi, Zahra Nikkhooy, and Masoud Parash. Statistical analyses were performed by Mohamad Sabaghan, Kazem Alizadeh-Barzian, and Mehdi Jamshidi. The manuscript was written by Ali Jamshidi. Mohammad Amin Ghatee was responsible for editing the final manuscript and generating the GIS-based maps.

Data Availability Statement

All data supporting the findings of this study are included within the article.

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